--53. (New) A composition comprising two vectors, the first vector comprising a polynucleotide encoding the vesicular fusion factor 2 protein and the second vector comprising a polynucleotide encoding a heterologous target protein.

54. (New) The composition of claim 53, wherein the polynucleotide encoding the heterologous target protein further comprises a signal sequence. --

REMARKS

Claims 3-13, 14-23, 25-27, 29-34, 36-42 and 47-52 are presently pending and under examination. Claims 3, 9, 47 and 48 have been amended above and claim 8 has been cancelled. New claim 53 and 54 have been added herein.

Claim 3 has been amended to incorporate the elements of dependent claim 8, which has been cancelled herein. Claim 9 has been amended to reflect dependence on base claim 3 rather than on cancelled claim 8 from which it previously depended. Claims 47 and 48 have been amended to recite that the claimed polynucleotides encompass sequences encoding a heterologous target protein. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

New claim 53 is directed to a composition of at least two vectors, the first vector encompassing a polynucleotide encoding the vesicular fusion factor 2 protein and the second vector encompassing a polynucleotide encoding a heterologous

target protein. New claim 54 recites that the polynucleotide encoding the heterologous target protein contains a signal sequence. Support for new claims 53 and 54 can be found throughout the specification, for example at page 14, lines 18-20 and in Figure 1B.

Applicants have set forth above the amendment to the claims in clean format and, in Appendix A, with marked up amendments indicated with brackets and underlining.

Rejections under 35 U.S.C. § 101

Applicants respectfully traverse the rejection of claims 3-7, 11 and 12 under 35 U.S.C. § 101, as allegedly directed to non-statutory subject matter.

Applicants respectfully submit that this rejection has been rendered moot by the amendments proposed herein, which now recite that the polynucleotides encompass sequences encoding a heterologous target protein. Accordingly, Applicants request removal of the rejection of claims 3-7, 11 and 12 under 35 U.S.C. § 101.

Rejections under 35 U.S.C. § 112, first paragraph

A. Regarding Written Description

Applicants respectfully traverse the rejection of claims 3, 5-12, 14, 16-23, 25, 31-34, 36-42 and 46 under 35

U.S.C.§ 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. Based on cancellation of claim 8, this rejection has been rendered moot with regard to this claim.

The Office Action alleges that the specification does not provide a written description of conservative variations of a polynucleotide sequence encoding a Vff2p encompassing SEQ ID NO: 2. Applicants respectfully disagree for the reasons that follow.

> [T]he essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed.

In re Barker, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978).

Applicants submit that the specification provides sufficient written description for the full scope of the invention. The specification provides both teachings and guidance regarding the characteristics of nucleotide substitutions that can be made to a polynucleotide sequence without affecting the production of a functional protein. In particular, at page 9, lines 15-27, the specification discloses that such conservative variations that do not affect production of a functional Vff2p include codon changes that, due to the degeneracy of the genetic code, do not result in amino acid

substitutions. In the same section, the specification further teaches that nucleotides representing transcriptional as well as translational elements can be added to a polynucleotide sequence of the invention. The resulting polynucleotides represent such conservative variations that do not affect functionality of the encoded protein.

With regard to the protein, the specification similarly provides guidance as to what constitutes a conservative variation. The specification teaches, for example, at page 10, lines 11-30, that a variant can be prepared, for example, by making a conservative substitution to the amino acid sequence of Vff2p that results in a polypeptide having the same or improved qualities as compared to the native polypeptide. The specification teaches that a conservative substitution is the substitution of an amino acid with another amino acid having a similar side chain so as to allow for the overall peptide to retain its spatial conformation. Furthermore, at page 11, lines 1-11, the specification further describes additional amino acid substitutions that can be made to a polypeptide of the invention that can result in, for example, increased secretory properties or enhanced ease of linkage to other molecules. In addition, at page 11, lines 12-29, the specification provides even further description of the invention polypeptides by teaching that amino acids can be substituted based on consultation of a hydropathicity or hydrophilicity index.

With regard to the assertion that the specification does not teach a structure-function relationship, Applicants

respectfully direct the Examiner's attention to the specification, which teaches at page 12, lines 1-14, that homologous sequences have been identified have been identified in *S. pombe*, the nematode *C. elegans*, and the plant Arabidopsis *(A. thalania)*. In particular, the specification discloses that Vff2p has 36% identity (i.e., identical amino acids) and 56% homology with *S. pombe*; had 25% identity and 46% homology with Arabidopsis; and 24% identity and 40% homology with *C. elegans*. Therefore, in addition to providing the full amino acid and nucleotide sequences of Vff2p and its encoding nucleic acid, the specification describes to the skilled artisan that highly conserved sequences exist in diverse organisms. Applicants respectfully submit that the description provided regarding both structure and function is sufficient to show that the inventor's had possession of the invention as claimed.

In view of the teachings in the specification, Applicants maintain that the specification provides sufficient description and guidance to convey to one skilled in the art that Applicants were in possession of the claimed invention. Accordingly Applicants respectfully request that the Examiner remove the rejection of claims 8-10, 12, 14, 16-23, 25, 31-34, 37-42 and 46 under 35 U.S.C. § 112, first paragraph.

B. Regarding Enablement

The objection to the specification and corresponding rejection of claims 3-12, 14-23, 25-27, 29-34, 36-42 and 47-52, under 35 U.S.C. § 112, first paragraph, as allegedly lacking

enablement respectfully is traversed. Based on cancellation of claim 8, this rejection has been rendered moot with regard to this claims. For the reasons that follow, Applicants respectfully submit that the specification enables the full scope of the claimed invention.

In *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since **a considerable amount of experimentation is permissible**, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Id. (Emphasis added) (citing *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d at 1564, 37 U.S.P.Q.2d at 1623); see also *In re Wands*, 858 F.2d at 736-40, 8 U.S.P.Q.2d at 1403-07.

The Office Action asserts that, while enabling for the expression of Vff2 protein in secretory mutants for S. cerevisiae host cells, the specification does not provide enablement for a useful expression of Vff2 protein in any host cell (current Office Action, Paper No. 22, page 5, second paragraph).

Applicants respectfully point out that none of the claims presently under examination recite "useful expression of Vff2 protein in any host cell." Applicants are not required under the first paragraph of section 112 of the Code, to provide enablement for language not recited in the claims.

For example, claim 7 recites a promoter operatively linked to a sequence encoding the Vff2p wherein the promoter is a promoter that functions in a host cell to direct transcription of the sequence encoding the Vff2p. Thus, as presently pending, claim 7 recites a promoter that can direct transcription in **a** host cell and does not require a showing of promoters for **any** host cell to be enabled. The specification teaches, at page 4, lines 9-17, that *S. cerevisiae* secreted proteins have been shown to be expressed at a higher yield in hosts such as *P. pastoris* and *H. polymorpha*. Claim 12 further recites the host cells *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Pichia pastoris*, *Hansenula polymorpha*, or *Kluyveromyces lactis*.

The Office Action cites a number of scientific abstracts, without putting on the record the entire corresponding publications, to support the proposition that "a number of proteins have been shown to be non-functional across species of yeast." These general citations, **none of which appear to describe expression of a secretory protein in a host cell**, are used to support the allegation that one skilled in the art would have had to undertake undue experimentation in order to express a

polynucleotide encoding a Vff2p in a host cell, for example, *P. pastoris* and *H. polymorpha*. Applicants respectfully suggest that, absent specific evidence that Applicants' teachings are non-enabled for expression in a host cell of a polynucleotide encoding a Vff2p, the citation of abstracts directed to unrelated proteins, is not sufficient to sustain an enablement rejection. Applicants submit that, given the guidance provided by the specification, only standard and well-known techniques not requiring undue experimentation, would have been required to produce and test expression in a host cell of a polynucleotide encoding a Vff2p as recited in the claims and thus practice the invention methods.

Finally, the Office Action asserts that it is unclear from the specification what secretory mutants in non-*S. Cerevisiae* cells would be suitable for expressing a polynucleotide encoding a Vff2p (current Office Action, Paper No. 22, page 6, final three sentences). Applicants respectfully submit that the specification teaches a number of secretory mutants in S. cerevisiae, including *sec17-1, sec18-1, bet1-1, sec22-2, uso1-1, pex3-1, sed5-1, cdc48-2, sec7-5,* and *ypt1-3.28*. The specification further teaches and cites authority for the proposition that secretory mutants are functionally defective in one or more of the proteins involved in the yeast secretory pathway and that proteins of the secretory pathway are highly conserved (specification, page 14, lines 7-11; page 3, lines 6-13). Given that secretory mutants in many species had been identified and described in the art at the time the application was filed, undue experimentation would not have been required to

produce and test expression of a polynucleotide encoding a Vff2p in a candidate mutant host cell.

Applicants submit that, given the guidance provided by the specification, only standard and well-known techniques not requiring undue experimentation, would have been required to produce and test expression in a host cell of a polynucleotide encoding a Vff2p as recited in the claims and thus practice the invention methods. Accordingly, withdrawal of the objection to the specification and removal of the corresponding rejection of claims 3-12, 14-23, 25-27, 29-34, 36-42 and 47-52, under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully requested.

Rejections under 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 3-7, 11, 36, 47 and 48 under 35 U.S.C. § 102(b), as allegedly anticipated by EMBL entry SCL9476.

Applicants respectfully submit that this rejection has been rendered moot by the amendments proposed herein, which now recite that the polynucleotides encompass sequences encoding a heterologous target protein and allow for high yields of secretion of the heterologous protein. Similarly, claim 36 directed to an isolated vesicular fusion factor 2 protein (Vff2p) has been amended to further recite presence of a heterologous target protein. EMBL entry SCL9476 does not teach polynucleotide sequences that encompass sequences encoding a heterologous target

protein or Vff2 protein sequences that encompass a heterologous target protein. Accordingly, Applicants request removal of the rejection of 3-7, 11, 36, 47 and 48 under 35 U.S.C. § 102(b), as allegedly anticipated by EMBL entry SCL9476.

Rejections under 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 14-18, 22, 23, 25, 26, 29, 49 and 50 under 35 U.S.C. § 103(a), as allegedly rendered obvious by EMBL entry SCL9476, in view of Mannhaupt *et al.*, Gene 85: 303-311 (1989).

To establish a *prima facie* case of obviousness, the Office must show that the prior art would have suggested the claimed method to one of ordinary skill in the art and that it could have been carried out with a reasonable likelihood of success when viewed in the light of the prior art. *Brown & Williamson Tobacco v. Philip Morris*, 229 F.3d 1120, 1124 (Fed. Cir. 2000).

For the reasons set forth below, the assertion that it would have been obvious for one skilled in the art to combine the cited references to arrive at Applicants' claimed invention is not accompanied by the required showing of where the cited references disclose the desirability of making the specific combination that is Applicants' claimed invention. Establishing that the prior art would have suggested the claimed method requires an underlying factual showing of a suggestion, teaching, or motivation to combine the prior art references and is an

"essential evidentiary component of an obviousness holding." *Brown & Williamson Tobacco*, 229 F.3d at 1124-25 (quoting *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1351-52 (Fed.Cir.1998); see also *C.R. Bard* at 1351 (obviousness requires some suggestion, motivation, or teaching in the prior art where to select the components that the inventor selected and use them to make the new device); *In re* Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000) (there must be some motivation, suggestion or teaching in the prior art of the desirability of making the specific combination that was made by the applicant). The evidentiary showing must be clear and particular and broad conclusory statements about the teachings of the cited references, standing alone, are not "evidence." *Brown & Williamson Tobacco*, 229 F.3d at 1125 (quoting *In re* Dembiczak, 175 F.3d 994, 1000 (Fed.Cir. 1999), abrogated on other grounds by *In re* Gartside, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir.2000)).

In the current Office Action, there has been no underlying factual showing that it would have been obvious to one of ordinary skill in the art to have modified the cited references to obtain the specific combination of elements of the claimed invention. None of these references, alone or viewed together, disclose that it is desirable to prepare a polynucleotide expression vector encompassing a polynucleotide encoding a Vff2p. Nor is there a suggestion, motivation or teaching within the references to prepare a recombinant host cell encompassing a yeast cell genetically altered to express a protein encoded by a polynucleotide sequence encoding a functional Vff2p.

Notably, the EMBL:SCL9476 entry simply sets forth the sequence of *S. cerevisiae* chromosome IV cosmid 9476 and is not accompanied by any functional description such that there would have been no motivation for the skilled person to prepare a polynucleotide expression vector or recombinant host cell as provided by the claimed invention. Neither does combination with the secondary reference by Mannhaupt et al. provide a teaching or suggestion of the claimed invention. In particular, the Mannhaupt et al. reference discusses expression of TYR1, which encodes prephenate dehydrogenase, one of the tyrosine biosynthetic enzymes and provides no teaching or suggestion of the desireability of a Vff2 protein. Notably, the authors of Mannhaupt et al. describe expression of a nucleic acid sequence encoding an protein of known function. Applicants maintain that, in contrast to the Mannhaupt et al. reference with the tyrosine biosynthetic enzyme, there would have been no motivation to express the protein encoded by the nucleic acid sequence of *S. cerevisiae* chromosome IV cosmid 9476, which is not accompanied by any functional description. Accordingly, the Office has not established its burden of a clear and particular showing of a suggestion, motivation or teaching of the claimed combination.

One purpose of the evidentiary requirement for showing a suggestion, motivation or teaching of the claimed combination is to prevent impermissible hindsight reconstruction of the claimed invention based on Applicants' own disclosure. *C.R. Bard*, 157 F.3d at 1352; *In re* Dembiczak, 175 F.3d 994, 999 ("[c]ombining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's

disclosure as a blueprint for piecing together the prior art to defeat patentability - the essence of hindsight"). In *C.R. Bard*, a case on point with the issue presented in the pending Office Action, the Federal Circuit again validated the purpose of the long recognized evidentiary requirement to sustain an obvious finding. In determining the validity of patented biopsy needle assembly over the sole assertion that it arose from obvious adaptations of a single prior art needle assembly to accommodate a new biopsy gun design, the court admonished against hindsight reconstruction when it stated:

> The invention that was made, however, does not make itself obvious; that suggestion or teaching must come from the prior art.

See, e.g., Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F.2d 1044, 1051-52, 5 USPQ2d 1434, 1438 (Fed.Cir. 1988) (it is impermissible to reconstruct the claimed invention from selected pieces of prior art absent some suggestion, teaching, or motivation in the prior art to do so); *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed.Cir. 1985) (it is insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor); *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556, 225 USPQ 26, 31 (Fed.Cir. 1985) (the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination). The court went on to conclude that because no prior art provided a teaching, suggestion or motivation for the structure of the claimed needle assembly there

was, as a matter of law, an absence of an essential evidentiary component for an obviousness finding. *C.R. Bard* at 1352.

Similarly, the Office Action lacks the evidentiary support required to show obviousness of Applicants' claims directed to a polynucleotide expression vector encompassing a polynucleotide encoding a Vff2p or a recombinant host cell encompassing a yeast cell genetically altered to express a protein encoded by a polynucleotide sequence encoding a functional Vff2p. More is required for a showing of obviousness than merely finding prior art pieces that mechanically can be added together to supply the elements of the claimed invention. The Office Action cites no text in the references that provides a suggestion, motivation or teaching to rearrange the components the references to achieve the combination that is either a polynucleotide expression vector encompassing a polynucleotide encoding a Vff2p or a recombinant host cell encompassing a yeast cell genetically altered to express a protein encoded by a polynucleotide sequence encoding a functional Vff2p. In this regard, the reliance on "common knowledge and common sense" to fill the void for the required showing of a suggestion for a claimed combination of element does not substitute for the obligation to cite references to support an obviousness conclusion. *In re* Lee, *In re* Thrift, 298 F.3d 1357, 1364 (Fed. Cir. 2002). Without an evidentiary showing of how the references provide a motivation to be combined in order to arrive at the claimed invention, the obviousness rejection is based on nothing more than impermissible hindsight reconstruction based on reading Applicants' own invention.

Further with regard to hindsight, Applicants point out that of the many nucleic acid sequences contained in the particular EMBL database entry, which sets forth the sequence of *S. cerevisiae* chromosome IV, the skilled person would have had no motivation to select from the numerous choices the particular sequence without the benefit of Applicants' disclosure as to the functional significance of Vff2 protein.

In view of the above, Applicants respectfully request removal of the rejection of claims 14-18, 22, 23, 25, 26, 29, 49 and 50 under 35 U.S.C. § 103(a) as allegedly rendered obvious by EMBL entry SCL9476, in view of Mannhaupt *et al.*, Gene 85: 303-311 (1989).

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to contact the undersigned attorney with any questions related to this application.

Respectfully submitted,

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Appendix A

3. A polynucleotide comprising a sequence encoding a vesicular fusion factor 2 protein (Vff2p), comprising SEQ ID NO:2, or conservative variations thereof**, and further comprising a sequence encoding a heterologous target protein**.

4. A polynucleotide comprising SEQ ID NO:1 or a sequence encoding SEQ ID NO:2.

5. The polynucleotide of claim 3, wherein the protein is about 32 kD.

6. The polynucleotide of claim 3, further comprising a promoter operatively linked to the sequence encoding the Vff2p.

7. The polynucleotide of claim 6 wherein the promoter is a promoter that functions in a host cell to direct transcription of the sequence encoding the Vff2p.

[8. The polynucleotide of claim 3, further comprising a sequence encoding a heterologous target protein.]

9. The polynucleotide of claim **[8]** 3, further comprising a second promoter operably linked to the sequence encoding the target protein operably linked to a second promoter.

10. The polynucleotide of claim 9, wherein the second promoter is a promoter that functions in the host cell to direct transcription of the target protein.

11. The polynucleotide of claim 7, wherein the host cell is a yeast cell.

12. The polynucleotide of claim 11, wherein the yeast cell is a Saccharomyces cerevisiae, Schizosaccharomyces pombe, Yarrowia lipolytica, Pichia pastoris, Hansenula polymorpha, or Kluyveromyces lactis.

14. A polynucleotide expression vector comprising a polynucleotide encoding a Vff2p comprising SEQ ID NO:2 or conservative variations thereof.

15. An expression vector comprising SEQ ID NO:1, or a sequence encoding SEQ ID NO:2.

16. The expression vector of claim 14, wherein the protein is about 32 kD.

17. The expression vector of claim 14, further comprising a promoter sequence operatively linked to the sequence encoding the Vff2p.

18. The expression vector of claim 17 wherein the promoter is a promoter that functions in a host cell to direct transcription of the sequence encoding the Vff2p.

19. The expression vector of claim 14, further comprising a sequence encoding a heterologous target protein.

20. The expression vector of claim 19, wherein transcription of the target protein is directed by a second promoter.

21. The expression vector of claim 20, wherein the second promoter is a promoter that functions in the host cell to direct transcription of the target protein.

22. The expression vector of claim 18, wherein the host cell is a yeast cell.

23. The expression vector of claim 22, wherein the yeast is Saccharomyces cerevisiae, Schizosaccharomyces pombe, Yarrowia lipolytica, Pichia pastoris, Hansenula polymorpha, or Kluyveromyces lactis.

25. A recombinant host cell comprising a yeast cell genetically altered to express a protein encoded by a polynucleotide sequence encoding a functional Vff2p, wherein the Vff2p comprises SEQ ID NO:2 or conservative variations thereof.

26. A host cell comprising SEQ ID NO:1, or a sequence encoding SEQ ID NO:2.

27. The host cell of claim 25, further comprising a sequence encoding a heterologous target protein.

29. The host cell of claim 25, wherein the yeast cell is a Saccharomyces cerevisiae, Schizosaccharomyces pombe, Yarrowia lipolytica, Pichia pastoris, Hansenula polymorpha, or Kluyveromyces lactis cell.

30. The host cell of claim 25, wherein the host cell lacks a functional protein involved in the secretory pathway and/or involved in the required cellular machinery for membrane fusion, other than Vff2p.

31. A method for increasing cell growth of a yeast host cell, comprising introducing a polynucleotide sequence encoding Vff2p into the cell and culturing the cell, wherein the Vff2p comprises SEQ ID NO:2 or conservative variations thereof.

32. The method for increasing cell growth of a cell according to claim 31, wherein the host cell is cultured under conditions effective to allow expression of the Vff2p.

33. A method for increasing protein secretion from a yeast host cell, comprising introducing a polynucleotide sequence encoding Vff2p into the cell and culturing the cell, wherein the Vff2p comprises SEQ ID NO:2 or conservative variations thereof.

34. The method for increasing protein secretion from a cell according to claim 33, wherein the host cell is cultured under conditions effective to allow expression of the Vff2p.

36. An isolated vesicular fusion factor 2 protein comprising SEQ ID NO:2, or conservative variations thereof**, and further comprising a heterologous target protein**.

37. A method of selecting for a yeast secretory mutant cell containing a polynucleotide sequence encoding a Vff2p operably linked to a promoter, wherein the Vff2p comprises SEQ ID NO:2, or conservative variations thereof, the method comprising growing the yeast secretory mutant cell at a restrictive temperature of about 32-37 C, wherein the restrictive temperature selectively favors mutant cell growth.

38. The method of claim 37, wherein the temperature is at about 37 C.

39. The method of claim 37, wherein the secretory mutant cell is sec17-1, sec18-1, bet1-1, sec22-2, uso1-1, pex3-1, sed5-1, cdc48-2, sec7-5, or ypt1-3.28.

40. The method of claim 39, wherein the secretory mutant cell is sec17-1, sec18-1, bet1-1, sec22-2, uso1-1, or pex3-1.

41. The method of claim 40, wherein the secretory mutant cell is sec18-1.

42. The method of claim 37, wherein the polynucleotide further comprises a sequence encoding a heterologous target protein operably linked to a second promoter.

46. The method of claim 31, 33 or 37, wherein the yeast cell is a Saccharomyces cerevisiae, Schizosaccharomyces pombe, Yarrowia lipolytica, Pichia pastoris, Hansenula polymorpha, or Kluyveromyces lactis cell.

47. An isolated polynucleotide comprising a sequence encoding a vesicular fusion factor 2 protein comprising SEQ ID NO:2, **, and further comprising a sequence encoding a heterologous target protein,** wherein the vesicular fusion factor 2 protein increases Saccharomyces cerevisiae cell growth or protein expression.

48. An isolated polynucleotide comprising SEQ ID NO:1 encoding a vesicular fusion factor 2 protein that increases Saccharomyces cereviae cell growth or protein expression **, and further comprising a sequence encoding a heterologous target protein.**

49. A polynucleotide expression vector comprising a polynucleotide encoding a vesicular fusion factor 2 protein comprising SEQ ID NO:2, wherein the vesicular fusion factor 2 protein increases Saccharomyces cerevisiae cell growth or protein expression.

50. A recombinant host cell comprising a Saccharomyces cerevisiae cell genetically altered to express a protein encoded by a polynucleotide sequence encoding a vesicular fusion factor 2 protein comprising SEQ ID NO:2.

51. A method for increasing cell growth of a Saccharomyces cerevisiae host cell, comprising introducing a polynucleotide sequence encoding a vesicular fusion factor 2 protein comprising SEQ ID NO:2 into the cell and culturing the cell.

52. A method for increasing protein secretion from yeast host cell, comprising introducing a polynucleotide sequence encoding a vesicular fusion factor 2 protein comprising SEQ ID NO:2 into the cell and culturing the cell.

53. (New) A composition comprising two vectors, the first vector comprising a polynucleotide encoding the vesicular fusion factor 2 protein and the second vector comprising a polynucleotide encoding a heterologous target protein.

54. (New) The composition of claim 53, wherein the polynucleotide encoding the heterologous target protein further comprises a signal sequence.